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On 4-21-03

TOWNSEND and TOWNSEND and CREW LLP

By: Linda Shaffer

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m.m.  
5/2/03

PATENT  
Attorney Docket No.: 15280-261100  
Client Ref. No.: E-016-1996/0-US-24

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Hyun K. Kim, et al.

Application No.: 09/180,132

Filed: May 24, 1999

For: 21-SUBSTITUTED  
PROGESTERONE DERIVATIVES AS  
NEW ANTIPROGESTATIONAL  
AGENTS

Examiner: Barbara P. Badio

Art Unit: 1616

DECLARATION OF HYUN K. KIM,  
PH.D. UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

I, Hyun K. Kim, state and declare as follows:

1. All statements herein made of my own knowledge are true, and statements made on information or belief are believed to be true and correct.

2. I am currently a Chemist in the Contraception and Reproductive Health Branch of the Center for Population Research at the National Institute of Child Health and Human Development, a division of the National Institutes of Health, Bethesda, Maryland. I have been with the NIH since 1972; prior to that, I was a Senior Research Scientist at Bristol Laboratories in Syracuse, NY from 1970 to 1971; an Organic Research Chemist at Hess and Clark, a division of Richardson Merrell, Inc. in Ashland, OH from 1966 to 1969; and a Research Chemist at E.I. du Pont de Nemours and Co., in Parlin, NJ from 1965 to 1966.

3. I received a B.S. from Seoul National University in Seoul, Korea, where I was a University scholar, and received a Ph.D. in Medicinal Chemistry from the University of Michigan, under the late Dr. Fred F. Blicke. After that, I was a Postdoctoral Fellow at Vanderbilt University from June 1963 to July 1965. Attached hereto as Exhibit A is a true copy of my *curriculum vitae*.

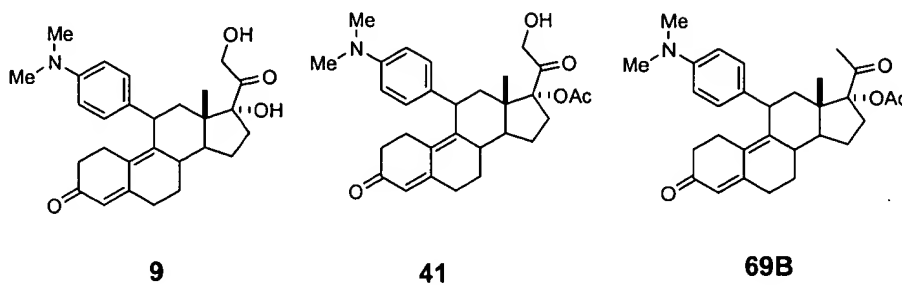
4. I am a named inventor on the above-referenced patent application. I have read and am familiar with the contents of this patent application. In addition, I have read the Office Actions, dated December 19, 2002 and November 5, 2001, received from the United States Patent & Trademark Office in the above-referenced patent application. It is my understanding that the Examiner is concerned that the compounds claimed are obvious in light of U.S. Patent No. 4,634,695 to Torelli, *et al.* (hereinafter Torelli). For the reasons set forth herein, the Examiner's concerns are overcome.

5. I first note that the compounds of Torelli are not encompassed by the claims of the present invention. The present invention relates to novel 11 $\beta$ -substituted-21-substituted-19-nor-progesterone analogs which possess potent antiprogestational activity and *minimal* antiglucocorticoid activity. In sharp contrast to the present invention, the invention of Torelli relates to 19-nor steroids having *antiglucocorticoid* activity.

6. In the previously filed responses, it was noted that the compounds of Torelli are both structurally and functionally different from the presently claimed compounds. However, the Examiner found previous arguments to overcome Torelli not persuasive in the absence of unexpected and unobvious results. At this point, I would like to submit surprising results that demonstrates the unexpected and unobvious performance of the compounds of the present invention compared to the compounds cited in Torelli.

7. The attached graph (Exhibit B) shows the percent inhibition of progesterone-induced endometrial proliferation (McPhail index) following oral administration of compound 9 (Torelli), compound 41 of the present invention, and compound 69B (related U.S. Application No. 09/526,855), in the anti-Clauberg test. The graph demonstrates that while compounds 41 and 69B show an increasing amount of antiprogestational activity as the dose

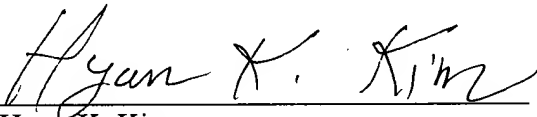
increases over a range of 2-8 mg, compound 9 shows **absolutely no activity** across the same range.



8. In my opinion, the absolute lack of antiprogestational activity of compound 9 would **not** motivate one of skill in the art to prepare the compounds of the present invention, including compound 41, for use as antiprogestational compounds.

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: March 31, 2003

  
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Hyun K. Kim